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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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DORSEY & WHITNEY LLP
INTELLECTUAL PROPERTY DEPARTMENT
4 EMBARCADERO CENTER
SUITE 3400
SAN FRANCISCO, CA 94111

EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,247	DEAR ET AL.	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9 and 16-23* is/are pending in the application.

4a) Of the above claim(s) *19,20,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8, 9, 16-18, and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 May 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 8, 9, 16-18, and 21 are under consideration in this Office Action.

2. The rejection of claims 8, 9, 16-18, and 21 under 35 U.S.C. 112, second paragraph, as being indefinite for being indefinite and omitting essential method steps have been withdrawn in view of applicants amendments to the claims.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 8, 9, 16-18, and 21 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility as stated in the previous Office Action.

Applicants' arguments filed 06/30/2004, have been fully considered but they are not persuasive. Applicant's position is that the asserted utility for the claimed method is for the reduction of normal or strong keratinization of hair which is based on the overexpression of the protease-related protein of the invention and underexpression of keratins Ha3 and CK15. The Examiner respectfully disagrees for reasons of record as supplemented below.

The "protease-related protein" recited in the claims is essential to the claimed method, where the said protease-related protein has the amino acid sequence of SEQ ID NO:2, is encoded by the polynucleotide of SEQ ID NO: 1, and has homologies to a protease of the kallikrein family. While applicants have provided an asserted utitliy for the recited method, the claimed invention has no well established utility or no specific or substantial asserted utility

The specification does not disclose any enzyme assays that demonstrate that the protein having the deduced amino acid sequence of SEQ ID NO: 2 has protease activity. The specification does not disclose that any homology to a reference protein known in the art is a disclosure that the claimed protein automatically has the properties and biological function of the reference protein relied upon. Furthermore, the specification's assignment of the protein as "protease-related protein" is not a specific asserted utility, but is, instead, a general asserted utility since many proteins that are related in any manner (i.e., amino acid sequence and

structure) to "protease-related protein" would be included. Although the specification teaches that when the whn gene product is absent then the Ha3 and CK15 are underexpressed and the polynucleotide encoding the "protease-related protein" is overexpressed, such correlation does not indicate any causal relationship where overexpression of "protease-related protein" promotes loss or lack of hair.

The state of the state of the art in protein function prediction from protein amino acid sequence and structure is reviewed by Whisstock et al. (Q Rev Biophys. 2003 Aug;36(3):307-40). Whisstock et al. teach (1) protein function prediction is a difficult problem since homologous proteins often have different and multiple functions; (2) methods for inferring function based on similarity in sequence and/or structure between an unknown protein and one or more well-understood proteins is tenuous and only provide guesses at function; (3) protein function predictions suggest function but do not determine function; (4) the most useful effect of protein function prediction is to guide laboratory experimentation to confirm, refute, or correct the prediction; and (5) protein function prediction from protein sequence and structure is useful but is not a substitute for laboratory experimentation (see entire publication, especially pp. 321-335).

A "specific utility" is specific to the subject matter claimed which contrasts with a general utility that would be applicable to the broad class of the invention. "Substantial utility" is one that provides a specific benefit in currently available form at the time of filing of the invention. Utilities that require or constitute carrying out further research to identify and/or reasonably confirm a specific use are not substantial and do not provide a specific benefit. See MPEP 2107.01

In view of the disclosure and state of the art in protein function prediction stated above, one of ordinary skill in the art would not recognize that claims 8, 9, 16-18, and 21 have a specific or substantial asserted utility or a well established utility since the only recognized utility of the claimed nucleic acid molecule and protein is to carry out further research to identify and/or reasonably confirm the specific biological function associated with the claimed nucleic acid molecule and protein. Since the claimed nucleic acid and protein lack utility, then the method for using the "protease-related protein" also lack utility.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 8, 9, 16-18, and 21 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above in the previous Office Action and in the rejection of claims 8, 9, 16-18, and 21 under 35 U.S.C. 101, one skilled in the art clearly would not know how to use the claimed invention.

In regard to claims 8, 9, 16, 17, and 18 encompassing any nucleotide sequence which hybridizes to SEQ ID NO: 1 at 20°C below the DNA melting which were rejected in the previous Office Action for lack of enablement, applicants traverse the rejection in arguments filed 06/30/2004, where applicants assert that one of skill in the art would be able to determine without undue experimentation whether variants encompassed by the claims could be used in the claimed invention by using methods to detect the change in chemical composition of hair. The Examiner respectfully disagrees for reasons of record as supplemented below.

Teachings regarding screening and searching for the claimed invention is not guidance for making the claimed invention. In order to make the claimed invention one of ordinary skill in the art must perform an enormous and undue amount of trial and error experimentation since the specification does not teach the specific structural/catalytic amino acids and the structural motifs essential for protein activity/function which cannot be altered. Such experimentation entails screening and searching a vast number of polynucleotides "hybridizes to SEQ ID NO: 1 at 20°C below the DNA melting" and determining whether the polynucleotide encodes the claimed "protease-related protein".

In arguments filed 06/30/2004, applicants further argue that *in vivo* data are not required to meet the enablement requirement, and that applicants assert that there is a causal relationship between the presence of the "protease-related protein" of the invention and the absence of hair. The Examiner respectfully disagrees for reasons of record as supplemented below.

It cannot be predicted whether administering the "protease-related protein" of the invention will result in reduction of normal or strong keratinization of hair the since there is no specific or substantial utility or well established utility for the said "protease-related protein". The more unpredictable the area is, the more specific enablement is necessary. If the specification disclosed *in vivo* working examples to show this, then this may overcome the enablement rejection. However, since the specification does not show any *in vivo* working examples, it is not clear that the claimed method is enabled.

There is no indication that the "protease-related protein" of the invention affects the

expression of the keratins Ha3 and CK15. The specification states that the whn gene is responsible for regulating the expression of the keratins Ha3 and CK15 and the "protease-related protein" of the invention, where absence of this whn gene results in underexpression of Ha3 and CK15 and overexpression of the "protease-related protein" (see p. 2, lines 16-22). There are no working examples to show that overexpressing the "protease-related protein" of the invention in skin host cells having an intact whn gene results in underexpression of Ha3 and CK15. In view of this, one of skill in the art would recognize that there is only a correlation between the whn gene and expression of Ha3, CK15, and the "protease-related protein" of the invention.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Conclusion

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally b`e reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christian L Fronda
Patent Examiner
Art Unit 1652

Majunath Rao
Primary Patent Examiner
Art Unit 1652